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New priorities: Analysis of the New Kidney Allocation System on UCLA patients transplanted from the deceased donor waitlist

Michelle J. Hickey [a,*], Ying Zheng [a], Nicole Valenzuela [a], Qiuheng Zhang [a], Carolyn Krystal [a], Erik Lum [e], Eileen W. Tsai [b], Gerald S. Lipshutz [c,d,e], H. Albin Gritsch [e], Gabriel Danovitch [e], Jeffrey Veale [e], David Gjertson [a], Michael Cecka [a], Elaine F. Reed [a]

[a] UCLA Immunogenetics Center, Department of Pathology and Laboratory Medicine, University of California, Los Angeles, CA, USA
[b] Department of Pediatrics, Division of Nephrology, David Geffen School of Medicine at UCLA, University of California, Los Angeles, CA, USA
[c] Department of Surgery, David Geffen School of Medicine at UCLA, University of California, Los Angeles, CA, USA
[d] Department of Urology, David Geffen School of Medicine at UCLA, University of California, Los Angeles, CA, USA
[e] Department of Medicine, David Geffen School of Medicine at UCLA, University of California, Los Angeles, CA, USA

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ABSTRACT

UNOS implemented a new Kidney Allocation System (New KAS) on December 4, 2014 with a primary goal of increasing equity to organ transplant for patients that were immunologically or socially disadvantaged by the previous allocation system (Previous KAS) that prioritized long wait times. We examined the effects of the New KAS on patients transplanted from the UCLA deceased donor waitlist during the first year and compared to the last year of the Previous KAS. The total number of deceased donor kidney transplants was increased in the New KAS as compared to the Previous KAS (178 vs 148). Transplant of regraft patients and of highly sensitized patients with cPRA $\geqslant$ 99% was significantly increased in the New KAS (New KAS vs Previous KAS, 29.8% vs 11.5%, $p \leqslant 0.0001$, and 26.4% vs 2.7%, $p \leqslant 0.0001$, respectively). In the New KAS, the percentage of patient's receiving allografts imported from outside our local area was also significantly increased (34.8% vs 15.5%, $p < 0.0001$). In the New KAS, 59.7% and 48.3% of imported organs were allocated to very highly sensitized ($\geqslant$99% cPRA) or re-graft patients, respectively, as compared to 8.7% and 8.7% during the Previous KAS ($p < 0.001$). Recipients and donors with age differences exceeding 15 years were decreased in the New KAS as compared to the Previous KAS (36.5 vs 48.7%, $p \leqslant 0.032$). There was a 40.1% reduction in transplant to patients in the 65+ age group in the New KAS ($p \leqslant 0.025$). The percentage of patients transplanted with preformed donor specific antibody (DSA) was similar in the New as compared to the Previous KAS (19.7% vs 15.5%) and, patients were transplanted with a range of 1–3 preformed DSA of weak to moderate strength. Cold ischemic time was significantly increased over all organs, and in patients transplanted with preformed DSA during the New as compared to the Previous KAS (17.5 vs 19.1 h and 17.2 vs 22.2, $p < 0.04$ and $p < 0.03$, respectively). Episodes of delayed graft function and the number of biopsies for cause were similar between the New and the Previous KAS. However, there were more events of biopsy proven antibody mediated rejection in patients transplanted since the start of the New KAS. The data show that the New KAS is working at the center level as designed to better age match recipients and donors and to increase transplantation of very highly sensitized patients through broader sharing.

1. Introduction

In December 2014, UNOS initiated a new Kidney Allocation System (New KAS) to replace the previous allocation system (Previous KAS) established in 1987 [1,2]. The New KAS is designed to increase the median lifespan and allograft-year survival in transplant recipients and to improve transplant to patients who are

Abbreviations: ACR, acute cellular rejection; AMR, antibody mediated rejection; ATN, acute tubular necrosis; cPRA, calculated panel reactive antibody; DGF, delayed graft function; DSA, donor specific antibody; KAS, Kidney Allocation System; EPTS, estimated post transplant survival; KDPI, Kidney Donor Profile Index; MCS, median channel shift; OPTN, organ procurement and transplantation network; UNOS, united network for organ sharing.

* Corresponding author at: UCLA Immunogenetics Center, 1000 Veteran Ave, Los Angeles, CA 90024, USA.
E-mail address: mhickey@mednet.ucla.edu (M.J. Hickey).

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socially or immunologically disadvantaged by shortfalls of the Previous KAS that prioritized longer wait times [3,4]. The New KAS is predicted to improve access to transplants for patients who were disadvantaged by broad sensitization to HLA antigens or by delayed referral to transplant centers, and to limit age mismatch between expected recipient and donor kidney longevity thereby also reducing allograft discard rate.

Several core components have been built into the New KAS to achieve these goals [1]. First, patients and donors are risk stratified according to two new calculated parameters. The Estimated Post-Transplant Survival (EPTS) score ranks patients based on age, dialysis time, diabetes status and primary or regraft status. The Kidney Donor Profile Index (KDPI) ranks donors based on multiple parameters of age, size, clinical status and donation after circulatory death status. Lower percentage EPTS and KDPI are correlated with improved post-transplant survival. In the New KAS, "longevity matching" between patients and donors is achieved by prioritizing patients with EPTS $\leqslant$ 20% to receive kidneys from donors with KDPI $\leqslant$ 20%. The second component is the use of a sliding scale from which points are awarded based on calculated panel reactive antibody (cPRA) prioritizing candidates with high cPRA. A third component broadens sharing for patients with a cPRA $\geqslant$ 99%. Pediatric candidates in the New KAS maintain priority over adult candidates to receive local offers from donors with KDPI < 35%. To increase transplant of blood type B candidates, eligibility for transplant with A_2/A_2B donors is now implemented with the New KAS. Finally, wait time is awarded to recipients based on time spent on dialysis prior to being registered to the waitlist—a component that was piloted in our local area prior to the start of the New KAS.

Simulated projections of the New KAS indicated a potential for increase in transplant of candidates in the 18–49 age range, for those of blood type B, and those with a cPRA $\geqslant$ 99%, and fewer transplants for candidates > 50 years old and those of blood type A [1]. In addition, allocation to those hardest to transplant, that is, very highly sensitized patients, would be improved by allowing regional and national sharing for candidates with cPRA $\geqslant$ 99% and regional sharing of kidneys from donors with a KDPI $\geqslant$ 85% [1].

These projections have been largely substantiated at the national level in the monitoring reports presented by UNOS/OPTN [5–8]. Nationally, an increase in transplantation of African Americans is also reported. Lacking from the national data, however, is analysis of short term outcomes in patients transplanted with preformed donor specific antibody (DSA). Patients that are very highly sensitized with a cPRA > 99% make up ~6% of the UCLA active waitlist for deceased donor renal transplantation and represent those that are at highest risk for delayed graft function (DGF) and rejection. Evaluating the New KAS at the center level is also important to assure that the quality of a national system is met at the local level. In this report, we present the data from the first year of the New KAS in comparison to the Previous KAS at the center level.

2. Materials and methods

2.1. Demographics

Patients who underwent deceased donor kidney transplant at UCLA during the first year of the New KAS (12/4/2014 to 12/4/2015) were compared to those transplanted during the same time period in the previous year (Previous KAS, 12/4/2013 to 12/3/2014). For all patients, sex, age at time of transplant, blood group, cPRA, regraft status and EPTS scores were gathered from UNOS data. Additional demographic information was collected by reviewing the patient's medical records including race, induction therapy, immunosuppression, presence of DSA, DGF, biopsy results, donor/recipient HLA-A, B, DR, DQ mismatch and graft loss. Deceased donor KDPI, local or regional/national import status and cold ischemic time were also determined from UNOS data. This study was approved by the UCLA institutional review board.

2.2. Antibody screening

Pretransplant, patients were screened for antibodies to HLA Class I and II using Lifecodes Flow Luminex PRA (Life Codes, Norcross, GA). Negative sera were screened annually. Sera identified as positive were then tested by Single Antigen Bead assay using the One Lambda LABScreen kit (One Lambda, ThermoFisher, Waltham, MA) and antibody reactivity greater than or equal to 1000 MFI were considered positive [9]. HLA antibody strength and specificity were tested at least annually by single antigen in patients found to be sensitized to HLA antigens. Post transplant, patients are stratified into immune monitoring protocols based on the presence or absence of preformed DSA at the time of transplant. Post transplant single antigen bead testing is also performed at suspicion of rejection.

2.3. HLA typing and crossmatch

Patient and donor HLA typing was performed by molecular methods as previously described [9]. Complement dependent T and B cell cytotoxicity crossmatches and T and B cell flow cytometric crossmatches were performed on all patients prior to transplant. In some cases, prior to performing the CDC or flow crossmatches, sera were treated with DTT to remove IgM, or T and B cells were incubated with pronase to remove Fc receptors and CD20 [10,11]. The positive threshold for a T or B flow crossmatch with or without pronase treatment is 50 or 120 median channel shift (MCS), respectively [9].

2.4. Immunosuppression

Throughout the duration of the study, induction was primarily solumedrol and basiliximab or anti-thymocyte globulin. The use of IVIG to augment immunosuppression at the time of transplant is used in most patients with DSA that is identified within one year of transplant (current). For patients with historic DSA, the use of IVIG at the time of transplant is at the discretion of the attending nephrologist. Maintenance immunosuppression for patients transplanted during both the New and Previous KAS primarily consisted of triple therapy with tacrolimus, mycophenolate mofetil (MMF) and steroids.

2.5. Diagnosis of rejection

Renal biopsies are not performed by protocol, but for cause on suspicion of allograft rejection. Rejection was characterized by the Banff classification [12].

2.6. Statistical methods

Statistical analyses were performed using Stata software version 13 (StataCorp, College Station, TX). Comparisons for categorical variables such as age group, cPRA group, blood type and race were analyzed by Fisher's exact test. Continuous variables such as cold ischemia time and DSA strength were compared using the Wilcoxon rank sum test. All tests were two-sided. P-values $\leqslant$ 0.05 were considered significant.

3. Results

3.1. Patient demographics

During the first year of the New KAS 178 deceased donor kidney transplants were performed at UCLA while 148 transplants were performed during the last year of the Previous KAS (Table 1). Of these, there was one combined kidney/pancreas transplant during the Previous KAS, and two were performed during the New KAS. There were no significant differences between patients transplanted in the New KAS or the Previous KAS with respect to gender, race, blood group, or number of HLA-A, B, DR zero mismatch transplants (Table 1). In contrast to national data presented by OPTN/UNOS the percentage of African American candidates transplanted was not significantly affected at our center during the New KAS [8]. Furthermore, no donor blood group A_2/A_2B to recipient blood group B transplants were performed.

The New KAS has made significant impact with respect to the age of transplant recipients in comparison to the Previous KAS. The median age of patients transplanted during the New KAS at our center was 51.0 years (range 2–78 years) that is significantly lower than the median age of patients transplanted during the Previous KAS (56.0 years, range 2–80 years, $p < 0.01$, Table 1). The reduction in median age of transplant recipients is further evidenced when the patients are subdivided based on age group (Fig. 1a). The data show that there is a significant reduction in the percentage of patients transplanted in the 65+ age group in the New KAS, while transplants to patients in the 18–64 age range were increased ($p < 0.03$; Fig. 1a, Table 1). Although the numbers are small, transplant of pediatric patients in the 0–17 age range were similar our center in the New KAS as compared to the Previous KAS, 6.2% vs 4.1%, respectively (Fig. 1a).

The New KAS prioritizes the transplant of adult patients with an EPTS $\leqslant$ 20% to receive allografts from donors with KDPI $\leqslant$ 20% [1]. During the New KAS, 11.3% of transplanted adult patients with an EPTS $\leqslant$ 20% received an allograft from a donor with KDPI $\leqslant$ 20% (Table 1). Our center's data suggest that longevity matching is improved since the start of the New KAS. When evaluating all

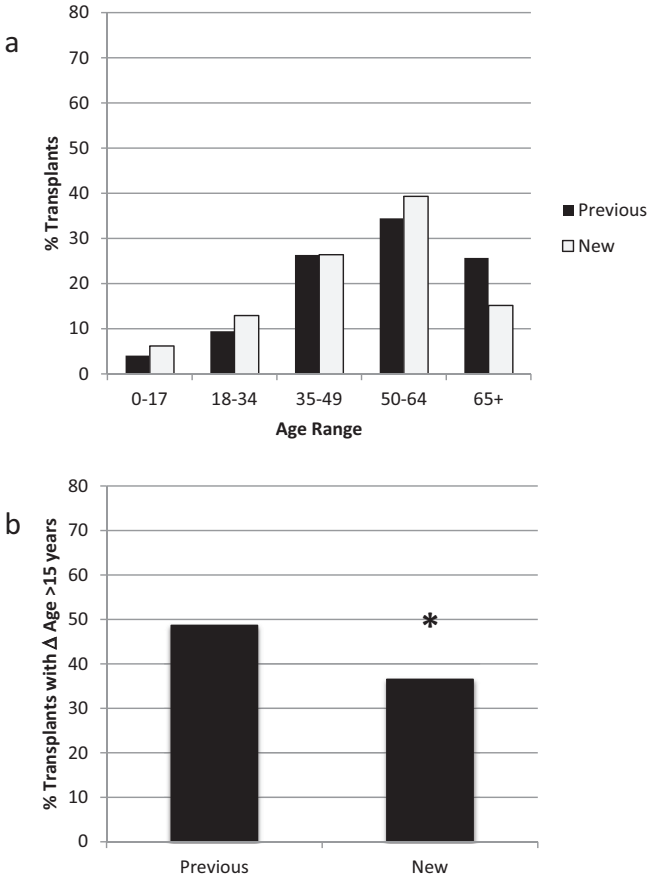

Fig. 1. Age of patients transplanted during Previous and New KAS. a) Patients transplanted during the New and Previous KAS grouped according to age (years). The percentage of patients transplanted in the age 65+ group is significantly reduced in the New KAS as compared to the Previous KAS ($p < 0.02$). b) Percentage of transplants with donor:recipient age difference >15 years in the New and Previous KAS.

Table 1
Transplant Demographics.

	Previous KAS		New KAS		*p*-value
	n	(%)	n	(%)	
Total number of transplants	148		178		
Sex	89	60.1	109	61.2	0.46
Age in years, median (range)	56 (2–80)		51 (2–78)		0.01
Age in years					
0–64	110	74.3	151	84.8	0.01
65+	38	25.7	27	15.2	
Race					
White	21	14.2	35	19.7	0.18
Black	32	21.6	33	19.9	
Hispanic	60	40.5	81	45.5	
Asian	31	21	22	12.4	
Other	4	2.7	7	3.9	
Blood Group					
A	50	33.8	54	30.3	0.34
B	20	13.5	28	15.7	
O	65	43.9	88	49.4	
AB	13	8.8	8	4.5	
Donor A2/A2B to Recipient B	–	–	0	0	
% KDPI, median (range)	47.5 (1–100)		50.5 (1–96)		0.95
KDPI $\leqslant$ 20% to EPTS < 20%	–	–	20	11.3	
Re-transplant	17	11.5	53	29.8	0.0001
% cPRA $\geqslant$ 98%	4	2.7	47	26.4	0.0001
Zero A B DR Mismatch	18	12.2	11	6.2	0.05
Cold time, hr, Av (range)	17.5 (4.0–40.0)		19.1 (5.3–42.9)		0.04
Graft Loss	3	2.0	1	0.6	

transplants, we find that there is a significant reduction in the percentage of recipient-donor pairs with an age difference > 15 years in the New KAS as compared to the Previous KAS (36.5% vs 48.6%, $p = 0.03$, Fig. 1b).

There is a significant shift in the New KAS toward transplant of patients who are very highly sensitized with cRPA ⩾ 98% ($p < 0.0001$, Table 1). Overall, 29.2% of patients transplanted at our center during the first year of the New KAS had a cPRA of 95–100%, and 23.6% were very highly sensitized with a cPRA of 99–100% (Fig. 2a). This is in striking contrast to the Previous KAS where only 2.0% of patients transplanted were very highly sensitized ($p < 0.0001$, Fig. 2a). Consequently, there was a measurable decrease in transplant of patients with a cPRA in the 0–79% range. Transplant of patients with a cPRA of 99–100% peaked at the start of the New KAS at 30.0%, and is longitudinally declining (Fig. 2b). Allocation of organs to patients receiving their second or third transplant is significantly increased at our center in the New KAS as compared to the Previous KAS ($p < 0.0001$, Table 1). The percentage of re-transplanted patients was increased nearly 3-fold in the New KAS as compared to the Previous KAS (29.8% vs 11.5%).

A core component of the new UNOS KAS is broader sharing of organs for patients that are very highly sensitized with a cPRA ⩾ 99% [1]. There was a 2-fold increase in patients transplanted with kidneys that were imported from outside of our service area in the New KAS as compared to the Previous KAS (34.8% vs 15.5%, $p = 0.0001$, Table 2).

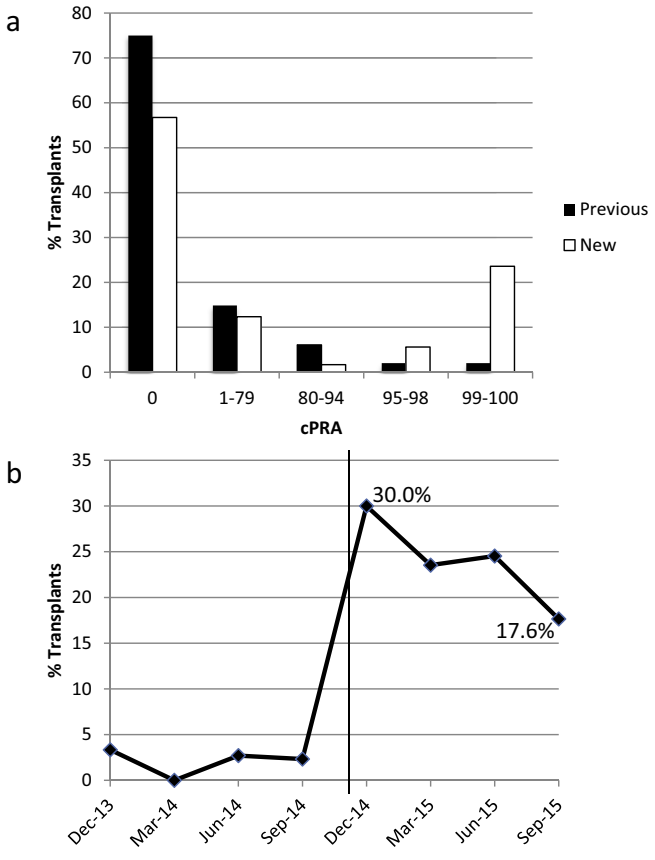

Fig. 2. cPRA of patients transplanted during the Previous and New KAS. a) Patients transplanted during the New and Previous KAS grouped according to cPRA. There is a significant shift toward transplant of very highly sensitized patients in the New KAS as compared to the Previous KAS ($p < 0.0001$). b) Quarterly, the percentage of patients transplanted with cPRA ⩾ 99% in the Previous and New KAS. Transplant of very highly sensitized patients peaked at the beginning of the New KAS (indicated by horizontal line) and is decreasing with time.

Characteristics of transplants with non-locally obtained organs were further evaluated (Table 2). During the New KAS our center saw 59.7% of imported kidneys allocated to very highly sensitized patients (cPRA ⩾ 99%, n = 37, Table 2), the majority of whom were also re-transplant patients (n = 30, 48.3%; Table 2). This is in contrast to the Previous KAS when only 8.7% (n = 2) imported allografts were allocated to patients with cPRA ⩾ 99% both of whom were re-transplant patients ($p < 0.0001$ and $p < 0.001$, respectively). The KDPI of imported organs allocated to patients in the Previous and New KAS according to patient cPRA was also evaluated (Table 2). In the New KAS, the average KDPI of imported organs allocated to patients with a cPRA of 0–98% was 62.1% (range 1–93%) and of grafts allocated to very highly sensitized patients was 41.8% (range 1–90%). During both the New and Previous KAS, allografts with a KDPI > 85% were primarily allocated to recipients with cPRA < 99%. Importantly, during the study period, all imported organs were transplanted to the patient for whom they were initially accepted.

3.2. Patients transplanted with preformed donor specific antibody

Studying the effects of the New KAS at the center level allows for evaluation of the presence of preformed donor specific antibody. The percentage of patients transplanted with preformed DSA in the New and Previous KAS was similar (19.7 vs 15.5; Table 3). Preformed antibody was classified either as current, meaning that it was present in the most recent serum tested by single antigen bead assay within one year prior to transplant, or as historic, meaning that it was absent in the most current serum yet present at some time during the patient's history. Among patients transplanted with preformed DSA, the DSA was present in the patient's serum at the time of transplant (current and current/historic) in 37.1% (n = 13) patients transplanted during the New KAS and in 65.2% (n = 15) patients transplanted during the Previous KAS. In addition, 71.4% (n = 25) patients in the New KAS were transplanted with historic DSA (historic and current/historic) in comparison to only 43.5% (n = 10) in the previous (Table 3). In the New and Previous KAS, patients were transplanted with a range of 1–3 DSA (Table 3). The range of strengths of preformed DSA present within one year prior to transplant is shown in Fig. 3. The median DSA strength between patients transplanted in the New and Previous KAS was similar (Previous KAS, median 2414 MFI [range: 1073–5805 MFI] and New KAS, median 3590 MFI [range: 1408 MFI-16353 MFI]), and statistical analysis shows that there is no distinction between the two groups ($p = 0.3$, Fig. 3) [13].

The use of immunosuppressive induction therapy augmented with IVIG was similar in this subset of patients during the New and Previous KAS (51.4% vs 60.9%, Table 3). Three patients in the New KAS with current preformed DSA had weak positive crossmatches in comparison to only one patient in the Previous KAS (Table 4). Two of the three positive crossmatches in the New KAS were for re-transplant patients with 100% cPRA that received kidneys imported from outside of our local area.

3.3. Cold ischemic time

A significant difference in cold ischemic time was noted overall on allografts transplanted during the New KAS as compared to the Previous KAS (19.1 vs 17.5 h, $p = 0.04$, Table 1). The cold ischemic time on organs imported from outside of our local area was similar in the Previous and New KAS (22.5 vs 22.6 h, Table 2). The cold time on imported allografts transplanted to very highly sensitized patients with cPRA ⩾ 99–100% was also similar in the Previous and New KAS (21.9 vs 21.7 h, Table 2). However, when evaluating the subset of patients transplanted with preformed DSA there is

Table 2
Transplants with Import Allografts (Recipients and Donors).

	Previous KAS		New KAS		*p*-value
	n = 148		n = 178		
n (%)	23 (15.5)		62 (34.8)		0.0001
Cold time, hr, Av (range)	22.5 (15.1–29.9)		22.6 (7.1–42.9)		0.93
	cPRA 0–98%	cPRA 99–100%	cPRA 0–98%	cPRA 99–100%	
n (%)	21 (91.3)	2 (8.7)	25 (40.3)	37 (59.7)	0.0001 *
Re-transplant, n (%)	3 (13.0)	2 (8.7)	2 (3.2)	30 (48.3)	0.001*
%KDPI, Av (range)	58.5 (23–93)	22	62.1 (1–93)	41.8 (1–90)	0.27*
KDPI ⩾ 85% (n)	3	0	6	1	
Cold time, hr, Av (range)	22.5 (15.1–29.9)	21.9 (19.3–24.6)	23.9 (12.8–42.9)	21.7 (7.1–42.7)	0.97*

* p value refers to comparison between patients with cPRA 99–100% in the Previous and New KAS.

Table 3
Transplants With Preformed DSA.

	Previous KAS n = 148		New KAS n = 178		*p*-value
	n	(%)	n	(%)	
Preformed DSA	23	15.5	35	19.7	0.38
Current	13		10		
Historic	8		22		
Current/Historic	2		3		
Class I	14		19		
Class II	8		10		
Class I/II	1		6		
Preformed DSA, Av (range)	1.3 (1–3)		1.2 (1–2)		
cPRA ⩾ 99%	1	4.4	20	57.1	0.0001
Cold time, hr, Av (range)	17.2 (4.0–31.9)		22.2 (7.1–42.7)		0.03
Import	0	0.0	19	54.2	0.0001
%KDPI, Av (range)	38.5 (4–90)		43.5 (1–90)		0.45
KDPI ⩾ 85% (n)	1		1		
IVIG	14	60.9	20	51.4	0.72
DGF	8	34.7	14	40.0	0.40
Biopsy for cause	11	47.8	12	34.3	0.41
ATN	7		8		
ACR	3		0		
AMR	1		3		
Other	0		1		

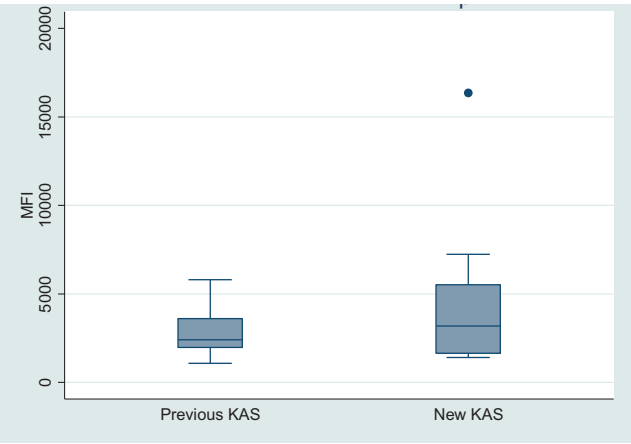

Fig. 3. Strength (MFI) of preformed DSA in sera tested within one year of transplant. Box and whisker plot shows range of preformed DSA strengths in the most current pre-transplant sera measured by single antigen bead test. Horizontal line indicates median (Previous KAS 2414 MFI, New KAS 3590 MFI). Box indicates upper and lower quartiles with whiskers showing the adjacent upper and lower values. One outlier is shown.

significantly increased cold ischemic time on organs from the New KAS as compared to the Previous KAS (22.7 vs 17.2 h, $p < 0.03$) as more than half of these grafts were imported from outside of our local area while none of the grafts were imported during the Previous KAS for this subset of patients (Table 3).

Table 4
Positive crossmatches in patients with current preformed DSA.

	Previous KAS	New KAS
1	T Flow: 49 MCS B Flow: 124 MCS DSA: A1 3220 MFI, A24 2435 MFI	T Flow: 18 MCS B Flow: 157 MCS DSA: DP10 4420 MFI
2	–	T Flow: 53 MCS B Flow: 103 MCS DSA: A3 1650 MFI, C7 2037 MFI
3	–	T Flow: 18 MCS B Flow: 124 MCS DSA: A11 2075 MFI

3.4. Short term outcomes in recipients with preformed DSA

Preformed DSA, cold ischemia time and donor quality are risk factors for delayed graft function (DGF) and rejection [14]. Defined as the need for dialysis during the first 7 days post-transplant, DGF was assessed in patients transplanted with preformed DSA during the New and Previous KAS. Although cold ischemic time was longer for allografts transplanted to patients with preformed DSA during the New KAS a similar percentage of patients experienced

DGF during the New and Previous KAS (40.0% vs 34.7%, $p = 0.40$, Table 3).

In patients transplanted with preformed DSA, there was no significant difference in the percentage of patients that underwent a biopsy for cause during the New and Previous KAS (Table 3). The majority of histopathological results were consistent with acute tubular necrosis (ATN). Three patients in this subset were found to have acute cellular rejection (ACR) during the Previous KAS. Although not statistically significant, there were more cases of biopsy proven antibody mediated rejection (AMR) during the New KAS as compared to the Previous KAS. The immunologic characteristics of AMR+ patients transplanted with preformed DSA are shown in Table 5. In total, 3 of the 4 patients were transplanted with a preformed DSA that was present historically, but not within one year prior to the transplant. One patient was transplanted during the New KAS with a DSA present within 4 months of the transplant date (Patient 4, current, DPB1*04:02, 7235 MFI). All 4 of these patients had negative crossmatches at the time of transplant. Only one patient had immunosuppression augmented with IVIG. Patient 4 was not treated with IVIG at the time of transplant as at that time the donor's DP typing was not known. All four cases of AMR occurred within one year post transplant, and three of the four occurred within 60 days of transplant. In all four patients, HLA DSA correlated to the AMR positive biopsy, and two of four patients had an expansion of HLA DSA with more DSA specificities present than previously noted. At the time of AMR, three patients were treated with plasmapheresis (PP) and IVIG or thymoglobulin. One patient was treated with IVIG and steroids and one patient received rituximab. There have been no events of graft loss in these four patients.

3.5. Graft loss

In patients transplanted during the Previous KAS, 3 allografts were lost (Table 1). In two of these, the graft was lost during the first week post transplant, followed by re-listing with the previous wait time and re-transplant during the New KAS. The third patient's graft failed approximately 1.5 years post transplant and the patient is currently relisted. One graft was lost from patients transplanted during the New KAS. The patient, transplanted with an organ isolated from a local donor with 23 h of cold ischemic time, was non-sensitized and experienced DGF and BK viremia post transplant. The graft failed after approximately 3 months, and the patient was relisted with their previous wait time and a cPRA of 100%. The patient was retransplanted during the study period with an organ imported from outside of our local area.

4. Discussion

The data from our single center experience in the first year of the New KAS show that the national UNOS Kidney Allocation System is working at the center level as designed to increase equity in access to renal transplantation. We evaluated the effects of major core components of the New KAS 1) broader sharing of organs for patients that are very highly sensitized, 2) patient:allograft longevity matching and 3) increased equity to candidates historically disadvantaged such as African Americans and other minorities. The data from our single center study also allows for analysis of allograft transplants to higher risk patients with preformed DSA.

Our findings, show that transplantation of very highly sensitized patients is increased more than 10-fold in the New KAS (Table 1, Fig. 1a) with nearly 60% of imported organs allocated to these patients (Table 2). This is in contrast to the Previous KAS, where the few imported organs were primarily allocated to patients with low cPRA. The 10-fold increase observed at our center is above the 4.5-fold increase observed nationally [8]. At our center, and nationally, transplant of very highly sensitized patents increased sharply during the first few weeks of the New KAS (Fig. 2b). Interestingly, at our center, the initial spike in transplant of very highly sensitized patents rose to ~30% of transplants, nearly double what was observed nationally. This so called "bolus effect" is hypothesized to be sustained by transplant of patients with common haplotypes leaving those with uncommon or homozygous typings perpetually listed. While nationally, the rate of transplantation of these patients appears to have stabilized at ~12%, the rate at our center continues to decline (Fig. 2b). At equilibrium, the New KAS offers a platform to study patient characteristics that lead to transplant vs death on the waitlist.

Similar to national data, we show improved longevity matching with the New KAS as recipients of allografts with patient:donor age differences > 15 years was significantly reduced (Fig. 1b) [8]. Furthermore, 11.3% of patients with EPTS < 20% received an allograft from a donor with KDPI < 20% (Table 1). With respect to transplant recipient age, we observed a significant, ~40%, reduction in transplant of patients >65 years that is greater than the ~20% reduction observed nationally (Table 1, Fig. 1a) [8]. The apparent enhanced effects of the New KAS at our center, discussed here and above, may correlate to the small number of transplants at our center,

Table 5
Immunologic characteristics of AMR positive patients transplanted with preformed DSA.

Patient No.	KAS	Current/ Historic	Preformed DSA Antigen	Immunosuppression	AMR		DSA		AMR Therapy
					Days post transplant	Rejection type	Antigen	MFI	
1	Previous	Historic	A24	Solumedrol/Thymo/ IVIG	12	Acute AMR, C4d+	A24	10235	PP × 5 days, IVIG
			A68				A68	5386	
							B35	10928	
							B39	10304	
2	New	Historic	DP2	Solumedrol/Thymo/ PP	54	Acute AMR, C4d+ [1]	B64	1214	PP 3× per week, IVIG, Ritux
							DR1	2954	
							DP402	4573	
							DP2	3878	
3	New	Historic	B37	Solumedrol/Thymo	310	AMR, C4d-, Suspicious for ACR	B37	6059	IVIG, Steroids
4	New	Current	DP402	Solumedrol/ Basiliximab	10	AMR, C4d-	DP402	3846	PP × 5 days, Thymo

1. Patient also had recurrent FSGS.

as compared to national numbers. Effects outside of the New KAS, such as center specific practice, may also contribute. Transplant of pediatric patients is similar at our center in the Previous and New KAS study periods (Fig. 1a) [8]. Although, nationally, after one year in the New KAS transplant of pediatric patients is similar to the Previous KAS, transplant of pediatrics in our region (Region 5) is reduced likely to the number of very highly sensitized patients listed for transplant and is hypothesized to recover after equilibrium is reached.

The data from our center are in contrast with parameters of the national data that report a statistically significant rise in transplant of African American patients and patients with blood type B. Nationally, transplant of African Americans increased significantly by ~17% in the New KAS [8]. This is likely a result of increased listing of this population of patients in preparation for the start of the new system, and of the core component that awards wait time points for time spent on dialysis prior to waitlist registration [1]. At our center, however, the percentage of whites and minorities transplanted was not different between the Previous and New KAS (Table 1). African Americans listed at our center for deceased donor renal transplant from June 2014 through March 2015, a period bridging the time when patients may have been added to the waitlist in preparation for the start of the New KAS, was stable at ~14% indicating referral of this ethnic group to our transplant center was not affected by the New KAS. Furthermore, our local area piloted the change in wait time from days since registration to the waitlist to days on dialysis. Therefore, at the start of the New KAS, we did not observe a bolus of patients transplanted due only to long dialysis time.

The national data also report a significant increase in transplant of blood type B recipients as a result of eligibility for A_2/A_2B donors [8]. However, this is due to the very modest total number of kidney transplants that have occurred nationally in this demographic (n = 109) since the start of the New KAS. At our center, no blood group B recipients are listed as eligible for a A_2/A_2B kidney donation. Successful deceased donor transplant of patients across ABO blood group requires considerable additional clinical management pre- and post-transplant [15]. The percentage of B kidneys in our local donor pool is too few to justify the cost of this pre-management and may explain the low percentage of patients nationally consented for this option [7].

Similar to national data, we show a significant increase in cold ischemic time over all organs since the start of the New KAS (Table 1) [8]. Cold ischemic time on organs transplanted to patients with preformed DSA during the New KAS was significantly increased as the majority of these were imported from outside of our local area (Table 3). Despite the increase in cold ischemic time, however, the percentage of patients transplanted with preformed DSA and experiencing DGF was similar between the New and Previous KAS (Table 3). Although there was no significant difference in the percentage of patients transplanted with preformed DSA during the New and Previous KAS there was a trend toward an increase in transplant across preformed DSA that were historic (Table 3, historic and current/historic, Previous KAS 43.5%, New KAS 71.4%). In the New KAS, these patients also tended to be very highly sensitized and were recipients of organs imported from outside our local area. While the percentage of "for cause" biopsies in patients transplanted with preformed DSA were similar (Table 3), there were more AMR positive biopsies in patients transplanted during the New KAS as compared to the Previous KAS (Tables 3 and 5). The immunologic features of patients with AMR positive biopsies were diverse with respect to DSA class and strength, proximity to transplant, immune induction therapy, and histologic features of AMR. Therapy at the time of AMR also differed, but included plasmapheresis in three of the four cases.

The success of the national KAS is due in large part to the advancement of solid phase assays and the ability to identify and block unacceptable antigens. With broader regional and national sharing of organs for highly sensitized patients as a core component of the New KAS, confidence in risk assessment by virtual crossmatch is essential. Our laboratory, and others, have experienced a significant increase in requests for virtual crossmatch since the start of the New KAS resulting in extensive modifications to staffing and laboratory workflow to accommodate the need. To improve the speed and accuracy of virtual crossmatch case review we also developed a computer program that assesses the patient's history of solid phase antibody tests for the presence of DSA prior to Director's review and risk assessment. This also allows for a reduction in manual review, and increased documentation and reporting to the electronic medical record. Our analysis indicates that 15–20% of patients are transplanted with at least one DSA of weak to moderate strength (1000–8000 MFI, Fig. 3). Virtual crossmatch prediction can be equivocal in the context of multiple weak DSA, or DSA near the unacceptable threshold [16]. However, only three very weak positive crossmatches were observed since the start of the New KAS (Table 4), and importantly, all organs imported during the New KAS were transplanted to the intended initial recipient. These data indicate that our strategies for identifying and blocking unacceptable antigens and assessing the presence/strength of donor specific antibody are satisfactory.

Still, it is important to consider the potential long term effects on graft outcome in transplanting patients across a strong DSA, even in the context of a negative crossmatch and augmented immunosuppression [17–19]. In the New KAS, one patient with 100% cPRA was transplanted with a DSA to DPB1*04:01 at 16363 MFI (Fig. 3), and a negative flow crossmatch, with an organ imported from outside of our local area. At the time of transplant, the patient was given immunosuppression with antithymocyte globulin augmented with a three-day course of IVIG. The patient experienced DGF during the first week post transplant. While the DSA to DPB1*04:01 was below the positive threshold by single antigen bead test 37 days post transplant, a weak DSA to B44 was identified. After two additional treatments with IVIG the patient is negative for HLA DSA. The patient has not had cause for biopsy during the short study period.

A total of four patients transplanted during the New KAS had only one DSA in serum current to the transplant that was to a DP antigen (Fig. 3). Two of these were to DPB1*04:01 (16353 MFI, Fig. 3 and discussed above, and 7235 MFI, Fig. 3 and Table 5, Patient 4), one was to DPB1*02:01 (6169 MFI, Fig. 3), and the last was to DPB1*10:01 (4420 MFI, Fig. 3 and Table 4). While, overall, there was no significant difference in strength of DSA current to the transplant in patients transplanted during the New and Previous KAS, three out four of these particular DSA exceeded the maximum strength of DSAs in the Previous KAS (Fig. 3, max 5805 MFI). Three of these four patients were treated with immunosuppression augmented with IVIG at the time of transplant. Cell surface expression of HLA DP is considered to be lower than expression of DR and DQ antigens [20]. DPB1*04:01 and DBB1*02:01 also carry the 496 A variant in the 3′UTR that is associated with even lower cell surface expression, potentially explaining the negative crossmatch in context of these moderate/strong DSA [21,22]. In contrast, the DSA to DPB1*10:01, carrying the 496 G variant, resulted in weak a positive crossmatch (Table 4). Since DP antigens can be entered as unacceptable on the UNOS waitlist it is important to consider antigen expression and DSA strength when evaluating the risk of transplant. Certainly, to improve patient care and avoid disadvantaging patients with strong DP DSA, more data is needed relating DSA strength to crossmatch results and graft outcome in patients transplanted with HLA DP antibodies. In addition, as one of these four transplants resulted in acute AMR (Table 4), long term outcomes

must also be assessed when transplanting across a DSA to DP, or antigen of another loci. Despite the lower expression of DP antigen on the cell, transplantation across a single DSA to DP is not without risk [18,19,23]. Furthermore, although transplanting patients with preformed DSA with immunosuppression augmented with IVIG results in significantly fewer rejection episodes it is not always effective and acute AMR remains an issue [24–26].

The New KAS provides great opportunity to transplant higher risk patients- those receiving their second or third transplant who are very highly sensitized with long dialysis times- and will result in fewer patients expiring while waitlisted on dialysis. However, if transplanting across DSA results in more rejections and earlier graft loss, then the ultimate goal of the New KAS, to increase graft and patient survival years will not be met. Longer term outcome data to assess these effects with an appropriate comparator group—very highly sensitized patients transplanted in the absence of DSA—is essential.

The New KAS appears to be working at the center and national levels to address shortfalls of the Previous KAS. Monitoring of national policy at the center level is essential to assess the effect on patient care and ensure quality is met. The New KAS prioritizes transplant of hardest to transplant patients—those who are very highly sensitized and likely to also have preformed DSA. Although short term outcomes of DGF, biopsies for cause and graft loss were similar between the New and Previous KAS at our center, long term outcomes must be evaluated to determine if the goal of increasing allograft and patient years is achieved through the New KAS.

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